PROC (BAYL UNIV MED CENT)
2021;34(6):678–680

https://doi.org/10.1080/08998280.2021.1941701

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# Contrast-associated acute kidney injury following peripheral angiography

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## ABSTRACT

Contrast-associated acute kidney injury (CA-AKI) is a well-known complication following angiography. Peripheral angiograms have been delayed or canceled for fear of worsening renal function leading to dialysis dependence. With the emergence of preventive measures, it is hypothesized that the risk of CA-AKI may be lower than previously observed. We performed a retrospective chart review of a single surgeon's 118 cases who underwent angiographic procedures from September 2019 through August 2020, recording patient characteristics and serum creatinine values. This cohort was comprised of 65 (55%) men and had a median age of 69 years [quartile 1 = 60, quartile 3 = 75]; 55 (47%) had diabetes mellitus and the median estimated glomerular filtration rate was 64 [45, 84] mL/min/1.73 $m^2$. We observed a statistically significant decrease in paired serum creatinine (-0.02 mg/dL) following the procedure, and only 4 patients (3.4%) developed CA-AKI, with older age and elevated baseline creatinine being associated with reduced kidney function. We did not detect an adverse relationship between contrast volume and CA-AKI. While CA-AKI continues to be a concern for patients who require peripheral angiographic procedures, this study found the overall risk to be low. This may be partly attributable to the use of pre- and postprocedure hydration protocols and lower contrast volumes.

**KEYWORDS** Acute kidney injury; angiography; contrast-associated acute kidney injury; estimated glomerular filtration rate; low-osmolar contrast media; serum creatinine

Contrast-associated acute kidney injury (CA-AKI), defined as a postprocedural peak serum creatinine (sCr) ≥1.5 times baseline sCr and/or a ≥0.3 mg/dL rise from baseline sCr, is an understood risk following angiography.[1] Factors that increase its likelihood include diabetes mellitus, preexisting chronic kidney disease, advanced age, intravascular volume depletion, a high volume of contrast administration, and use of nephrotoxic medications.[2] Conversely, preventive measures such as pre- and postprocedural intravenous isotonic crystalloid solution, use of low or iso-osmolar agents, and use of the lowest necessary volume of contrast may improve patient outcomes.[2] Emerging data suggest that the risk of CA-AKI may be lower than previously expected for patients treated under such protocols.[2] It was of interest to investigate the incidence of CA-AKI following angiographic procedures in a cohort of patients treated by a single physician at our institution. We hypothesized that there would be no significant difference between the preprocedure and postprocedure sCr and that a greater volume of contrast administration would be associated with decreased renal function.

## METHODS

We performed a retrospective chart review of a single surgeon's consecutive cases for 1 year, September 2019 through August 2020. We extracted demographics (age, gender, race), patient history and comorbidities (prior renal surgery, diabetes mellitus, body mass index), procedural information (procedure type, contrast volume), and laboratory values (preprocedural sCr, postprocedural sCr) from the electronic health record. While all angiographic cases during the study timeframe were eligible for inclusion, those with missing sCr values were excluded from analyses, as the primary aim of this work was to study kidney function before and after the procedure. As this work is descriptive in nature, we provide summary statistics in the form of median [quartile 1, quartile 3] for continuous variables (most were skewed), and frequencies and percentages for categorical

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The authors report no conflicts of interest.

Received May 19, 2021; Revised June 2, 2021; Accepted June 3, 2021.

Table 1. Patient characteristics (n = 118)

| Characteristic | Frequency (%); median [quartile 1, quartile 3] |
|---|---|
| Men | 65 (55%) |
| Age (years) | 69 [60, 75] |
| Black | 33 (28%) |
| White | 68 (58%) |
| Hispanic | 17 (14%) |
| Body mass index (kg/m$^2$) | 27 [23, 33] |
| Diabetes mellitus | 55 (47%) |
| Prior renal surgery | 5 (4%) |
| Contrast volume (mL) | 75 [50, 120] |
| Preprocedural serum creatinine (mg/dL) | 1.09 [0.87, 1.45] |
| Postprocedural serum creatinine (mg/dL) | 1.05 [0.9, 1.41] |
| Paired change in serum creatinine (mg/dL)[a] | −0.02 [-0.16, 0.08] |
| Preprocedural eGFR (mL/min/1.73 m$^2$) | 64 [45, 84] |
| Postprocedural eGFR (mL/min/1.73 m$^2$) | 67 [49, 85] |
| Contrast-associated acute kidney injury | 4 (3%) |

eGFR, estimated glomerular filtration rate.
[a]Change in serum creatinine taken as post – pre.

variables. We evaluated patient and procedural characteristics associated with postprocedural kidney function by considering postprocedural sCr, postprocedural estimated glomerular filtration rate (eGFR; calculated using the CKD-EPI formula), and postprocedural contrast-associated acute kidney injury ($\geq$1.5× baseline sCr and/or $\geq$0.3 mg/dL rise from baseline sCr).[1]

We utilized Pearson's or Spearman's correlation coefficient, as appropriate, to assess the correlation between postprocedural kidney function (sCr and eGFR) and continuous factors (age, preprocedural sCr and eGFR, contrast volume, body mass index) and the Wilcoxon rank sum test to assess the relationship between postprocedural sCr and categorical factors (gender, race, diabetes mellitus, prior renal surgery). We utilized the Wilcoxon signed rank test to determine whether significant changes in paired kidney function (sCr, eGFR) occurred following the procedure. Ultimately, we did not perform statistical tests for associations with CA-AKI due to the small event count.

## RESULTS

A total of 156 cases were identified during the study timeframe, 38 (24%) of which were excluded from analyses due to missing postprocedural sCr. The median age of the 118 cases was 69 [60, 75] years; 65 (55%) were men, and 55 (47%) had diabetes mellitus *(Table 1)*. Baseline sCr and eGFR revealed a range of kidney function among the patients in our study, with the median kidney function being normal to mildly decreased. The median contrast administered during the procedure was 75 [50, 120] mL. We observed a significant improvement in the paired change of sCr (–0.02 [–0.16, 0.08] mL, $P = 0.03$), but did not detect a difference in paired eGFR (0.62 [–4.52, 7.78], $P = 0.08$). Only 4 (3.4%) patients developed CA-AKI.

The patient characteristic most closely associated with postprocedural kidney function was preprocedural kidney function (correlation between pre- and postprocedure sCr: 0.94, $P < 0.0001$, *Figure 1a*; correlation between pre- and postprocedure eGFR: 0.94, $P < 0.0001$, *Figure 1b*). Older age was another factor that was generally associated with worse kidney function, with a significant negative correlation ($r = -0.53$, $P < 0.0001$) with postprocedural eGFR and a trend toward significance with higher postprocedural sCr ($r = 0.13$, $P = 0.15$). There was not a significant relationship between contrast volume and postprocedural sCr or eGFR *(Table 2)*. Postprocedural kidney function did not differ based on gender, race, or diabetes ($P > 0.05$). In a multivariable model to consider the joint effect of patient characteristics on postprocedural sCr, the only variable that significantly contributed to the model was preprocedural sCr.

## DISCUSSION

Acute kidney injury (AKI) following intravenous contrast administration was first characterized in 1954 when a patient progressed into acute renal failure following an intravenous pyelogram.[3] Since then, one of the most significant protections against CA-AKI has been the transition from high-osmolarity contrast to low-osmolar or iso-osmolar contrast media.[3] Early contrast media had osmolarities reaching 2200 mOsm/kg, which represents 5 to 8 times the osmolarity of any tissue or fluid in the human body.[4] This drastic change in osmolarity can deform red blood cells, cause direct injury to vascular endothelial cells, and result in shifts in the intravascular and extravascular fluid volume.[4] Further, it can cause widespread vasodilation and conversely renal artery vasoconstriction.[4] Low-osmolar contrast media was developed in 1974 with an osmolarity ranging from 780 to 800 mOsm/kg.[4] Although this is hyperosmolar compared to the average serum osmolarity of 300 mOsm/kg, it is still a 64.1% reduction in osmolarity from the previous high osmolarity of contrast media used.[4] Luk and colleagues observed more than a threefold protection against nephropathy in patients treated with low-osmolar when compared to high-osmolar contrast agents.[3] The low rate of CA-AKI observed in our study may be partly attributable to the avoidance of high-osmolar agents at our center; low-osmolar contrast media is used in most cases and iso-osmolar contrast media is used for high-risk patients.[5]

Another strategy to combat CA-AKI is the use of a pre- and postprocedural intravenous hydration, which maintains adequate intravascular volume.[6] Current recommendations include beginning a 1 mL/kg/h infusion of normal saline for 6 to 12 hours prior to the procedure, as well as continuing the infusion intraprocedure and 6 to 12 hours postprocedure.[2,6] Other medications such as N-acetylcysteine, sodium

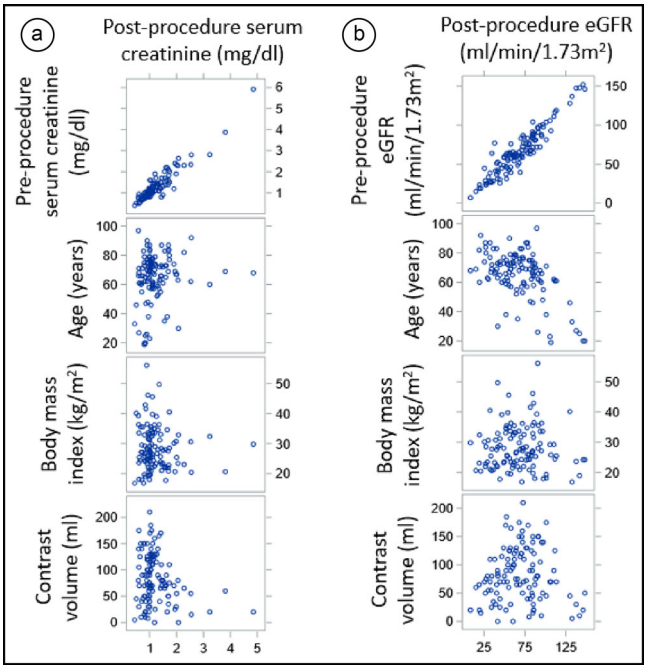


**Figure 1.** Scatterplot matrix of postprocedural **(a)** serum creatinine and **(b)** estimated glomerular filtration rate (eGFR) with eGFR/serum creatinine, age, body mass index, and contrast volume for 118 patients undergoing angiographic procedures.

**Table 2. Correlations (*P* values) between continuous variables and measures of kidney function in 118 patients undergoing angiographic procedures**

| Variable | Serum creatinine | eGFR |
|---|---|---|
| Preprocedure serum creatinine | 0.94 (<0.0001) | −0.68 (<0.0001) |
| Preprocedure eGFR | −0.68 (<0.0001) | 0.94 (<0.0001) |
| Age | 0.15 (0.11) | −0.53 (<0.0001) |
| Body mass index | −0.05 (0.56) | 0.03 (0.72) |
| Contrast volume | −0.09 (0.35) | 0.05 (0.58) |

eGFR indicates estimated glomerular filtration rate.

bicarbonate, and alprostadil have also been evaluated for protection against CA-AKI, but their efficacy remains controversial.[2,4,6,7] While physicians in our vascular department administer pre- and post-hydration for angiographic procedures on a per-case basis, there is not a standardized hydration protocol, which we recognize as a confounding variable that can affect postprocedure sCr.

Using >30 mL of low-osmolar contrast media has been associated with an increased incidence of CI-AKI.[8] As 75% of our cases received at least 50 mL of contrast, it was surprising to see a general trend of improvement in sCr following the procedure. One potential explanation is the intravenous fluid administered before, throughout, and after the procedure on a case-by-case basis. Additionally, most patients in this study had normal baseline kidney function, which decreases the risk of CA-AKI.

Our retrospective study is not without limitations. There is potential bias in this study due to the exclusion of 24% of subjects who did not have sCr measured following the procedure; however, we believe that CA-AKI was unlikely in those cases because the patients quickly met criteria for discharge and did not have any adverse kidney events that we were aware of or reported when seen for follow-up visit. Further, there were no differences in baseline kidney function between those who did vs did not have postprocedural laboratory data available (sCr $P = 0.5$, eGFR $P = 0.38$). For those with available data, it is unknown whether the true peak of postprocedural sCr was captured in this study, as patients were not under additional medical or laboratory observation following discharge. It has been shown that sCr typically peaks within 2 to 3 days of a known insult, and baseline kidney function returns within 7 to 10 days, which could also be a confounding factor in our study.[2] Another limitation is that we did not record data on hydration methods.

In conclusion, CA-AKI is a risk of angiography that may prevent some patients from receiving necessary diagnostic and interventional endovascular procedures. This study suggests that the greatest predictor of postprocedural kidney function is preprocedural kidney function. With judicious contrast administration and the use of hydration before and after the procedure, the risk of CA-AKI can be reduced, particularly for those patients with impaired baseline kidney function.

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